

Please replace the paragraph beginning at page 37, line 21 with the following:

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--cDNA libraries constructed with the SuperScript Plasmid System for cDNA Synthesis and Plasmid Cloning (GIBCO-BRL, Rockville MD) using mRNA from mitoxantrone resistant S1-M1-80 human colon carcinoma cells can be used to isolate the MXR1 nucleic acids of the invention.--

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Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 8, at the end of the application.

In the Claims:

Please amend claims 1-3, 7-13, 17 and 18 as follows:

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1. (Amended) An isolated ATP-binding cassette protein having the following properties:
 - i. conferring mitoxantrone resistance to a S1-M1-80 human colon carcinoma cells when expressed in the cells; and,
 - ii. specifically binding to polyclonal antibodies which specifically bind to a member of the group of proteins depicted in SEQ ID NO:2 or SEQ ID NO:4; and
 - iii. having a molecular weight between about 70 kDa and about 75 kDa.

2. (Amended) The ATP-binding cassette protein of claim 1 wherein the protein has 95% identity to the amino acids depicted in SEQ ID NO:2 or SEQ ID NO:4.

3. (Amended) A eukaryote cell genetically altered to overexpress an ATP-binding cassette protein having the following properties:

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CONT. —
- i. conferring mitoxantrone resistance on S1-M1-80 human colon carcinoma cells when expressed in the cells; and,
 - ii. specifically binding to polyclonal antibodies which specifically bind to a member of the group of proteins depicted in SEQ ID NO:2 or SEQ ID NO:4.
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7. (Amended) A DNA encoding a ATP-binding cassette protein wherein the protein is characterized by having the following properties:

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- i. conferring mitoxantrone resistance on S1-M1-80 human colon carcinoma cells when expressed in the cells; and,
 - ii. specifically binding to polyclonal antibodies which specifically bind to a member of the group of proteins consisting of those depicted in SEQ ID NO:2 or SEQ ID NO:4.

8. (Amended) The DNA of claim 7, wherein the encoded protein has 95% identity to the amino acids depicted in SEQ ID NO:2 or SEQ ID NO:4.

9. (Amended) The DNA of claim 7, wherein the DNA encoding the protein has a sequence identical to that depicted in SEQ ID NO:1 or SEQ ID NO:3.

10. (Amended) A process for over expressing ATP-binding cassette protein in a cell comprising a first step of either:

- i. transforming the cell with an expression cassette which directs the expression of ATP-binding cassette protein; or,
- ii. selecting a cell having an endogenous copy of the ATP-binding cassette protein, and transforming the cell with DNA which can serve as an enhancing element or as a second promoter where the insertion is upstream of the endogenous promoter operatively linked to the ATP-binding cassette protein and where the inserted DNA increases the basal expression levels of ATP-binding cassette protein; and a second step of,

culturing the transformed cell under conditions where the levels of ATP-binding cassette protein are increased above the basal levels of the non-transformed cells with the proviso that the ATP-binding cassette protein has the following properties:

- a. confers mitoxantrone resistance on S1-M1-80 human colon carcinoma cells when expressed in the cells; and,
- b. specifically binds to polyclonal antibodies which specifically bind to a member of the group of proteins depicted in SEQ ID NO:2 or SEQ ID NO:4.

11. (Amended) The process of claim 10, wherein the ATP-binding cassette protein has 95% homology to the amino acids depicted in SEQ ID NO:2 or SEQ ID NO:4.

12. (Amended) The process of claim 10, wherein the protein has the amino acids depicted in SEQ ID NO:2 or SEQ ID NO:4.

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cont.

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13. (Amended) A method of screening for inhibitors of cytotoxin resistance in cells comprising the steps of :

(a) culturing a cell genetically altered by the introduction of heterologous DNA which permits the overexpression an ATP-binding cassette protein where the protein has the following properties:

- i. conferring mitoxantrone resistance on S1-M1-80 human colon carcinoma cells when expressed in the cells; and,
- ii. specifically binding to polyclonal antibodies which specifically bind to a member of the group of proteins depicted in SEQ ID NO:2 or SEQ ID NO:4;

(b) contacting the cell with a cytotoxin in an amount that permits cell survival due to the resistance conferred by the ATP-binding cassette protein;

(c) contacting the cell with a compound that inhibits the biological activity of the ATP-binding cassette protein;

(d) detecting the inhibition by measuring growth inhibition of the cells.

17. (Amended) A method of claim 13, wherein the ATP-binding cassette protein has 95% homology to the amino acids depicted in SEQ ID NO:2 or SEQ ID NO:4.

18. (Amended) A binding protein which specifically binds to an ATP-binding cassette protein which has 95% homology to the amino acids depicted in SEQ ID NO:2 or SEQ ID NO:4.